HPTN084

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iavi

2nd Annual PEPFAR Uganda Science Summit
Reaching and Maintaining Epidemic Control
January 2021
Kampala Uganda (virtual)

UGANDANS AND AMERICANS IN PARTNERSHIP TO FIGHT HIV/AIDS

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Project Title

HPTN 084:
A Phase 3 Double Blind Safety and Efficacy Study of Long-Acting Injectable Cabotegravir Compared to Daily Oral TDF/FTC for Pre-Exposure Prophylaxis in HIV-Uninfected Women.

2nd Annual PEPFAR Uganda Science Summit January 2021

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Primary Objectives

- Evaluate the efficacy of CAB LA versus TDF/FTC
- Evaluate the safety of CAB LA versus TDF/FTC

Secondary Objectives

- Compare HIV incidence among participants receiving CAB/CAB LA vs. TDF/FTC (Steps 1, 2 and 3)
- Evaluate relative efficacy of CAB/CAB LA vs. TDF/FTC in subgroups of: age, HSV-2 serostatus, contraceptive method, and BMI
- Describe and model the relationship between HIV incidence and drug concentration
- Describe the distribution and correlates of drug concentration
- Compare the acceptability of and preferences for CAB LA vs. oral TDF/FTC

HPTN084

- Population: women at-risk for acquiring HIV, ages 18y- 45y

- Study Duration:
  - 1.5 to 3.5 years of intervention
  - 1 year of follow-up

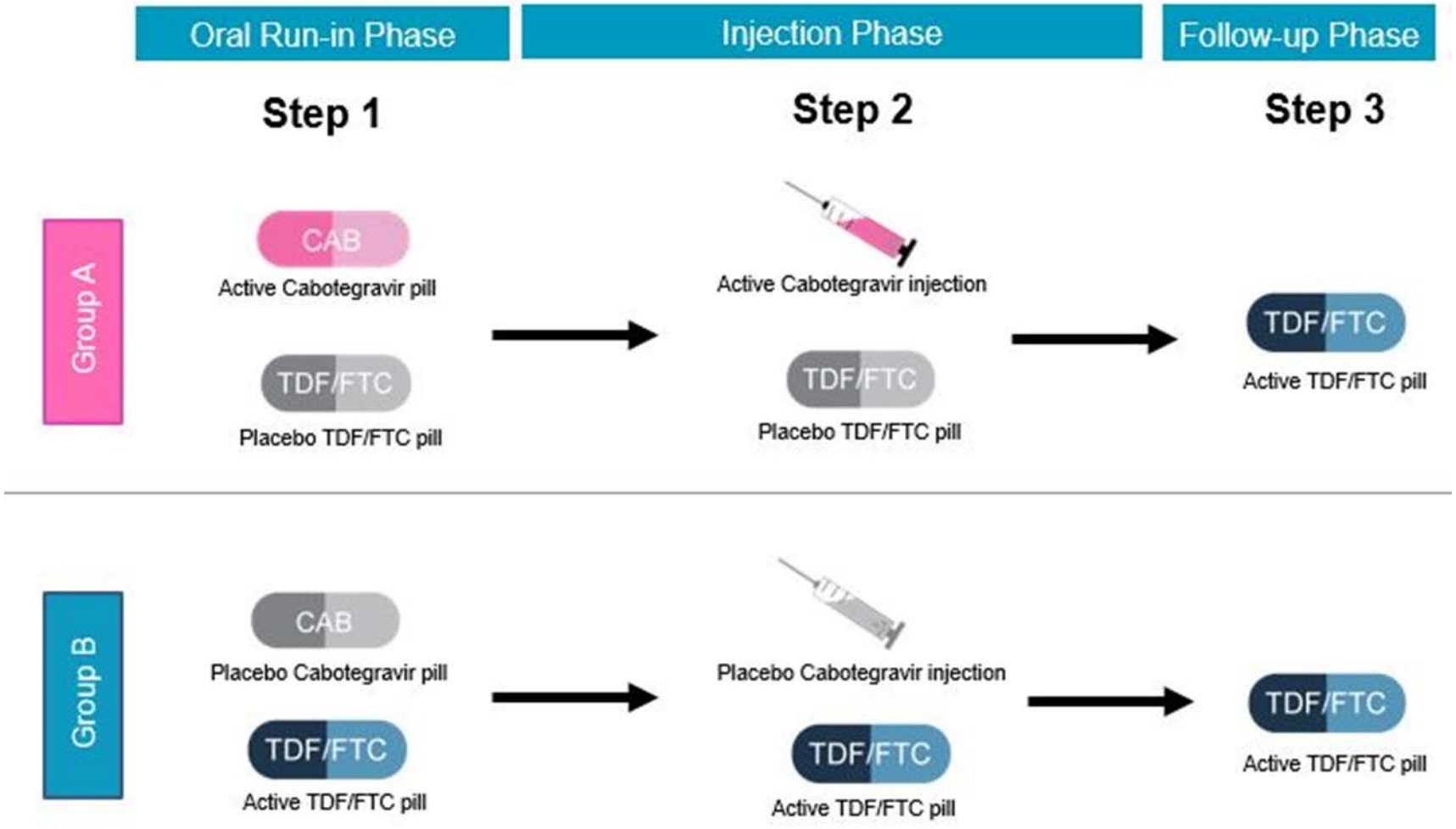
- Total Number enrolled: 3,224

- Number of sites:
  - 20 sites; Botswana, Eswatini, Kenya, Malawi, South Africa, Uganda (3 sites) and Zimbabwe.

Enrollment in Uganda

- Baylor-Uganda-
  - 210
  - Dr. Patricia Nahirya Ntege
- MUJHU
  - 204
  - Dr. Clemensia Nakabiito
- UVRI-IAVI
  - 182
  - Dr. Juliet Mpendo

Study Design



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HPTN084 DSMB Preliminary Results

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DSMB Press Release

- During a planned review of study data on 05 Nov 2020, an independent Data and Safety Monitoring Board (DSMB) recommended the study sponsor (NIH/NIAID/DAIDS) to stop the blinded phase of the trial and share the results.

- The HPTN 084 study is jointly-funded through a unique partnership between NIAID, the Bill & Melinda Gates Foundation, and ViiV Healthcare.

- Study drugs are provided by ViiV Healthcare and Gilead Sciences, Inc.

DSMB Press Release

- A total of 3,223 HIV uninfected participants were enrolled between 26 November 2017 and 5 November 2020.
- A total of 3,127 participants were included in the analysis at the time of the DSMB review.
- Overall, 1,566 participants were randomized to the CAB LA arm and 1,561 participants were randomized to the daily oral FTC/TDF arm.

Demographics

- The average age of study participants was 26 years and 57% of participants were 18-25 years old.
- 82% of the women enrolled were not living with a partner.
- 55% reported two or more partners in the past month.
- 34% having a primary partner who is reported to be living with HIV or having an unknown HIV status.

Efficacy Key Points

- The overall HIV incidence among all study participants was very LOW at 1.00% (95% CI 0.71 %-1 .37%), suggesting that both CAB LA and FTC/TDF are highly effective for HIV prevention in the HPTN 084 population.

- A total of 38 HIV infections have occurred during follow-up as of now.
  - 4 infections in the CAB LA arm (incidence rate 0.21 %)
  - 34 infections in the FTC/TDF arm (incidence rate 1.79%)
  - Approximately nine times more incident HIV infections occurred in the FTC/TDF arm than in the CAB arm.

- These results meet the statistical criteria for superiority of CAB LA compared to FTC/TDF in the HPTN 084 study population

Adherence

- The higher-than-expected level of adherence to FTC/TDF throughout the study and overall low incidence rate in both arms of the study clearly demonstrate both drugs were highly effective at preventing HIV acquisition.

Drug Concentrations and Adherence

- In a random sample of approximately 362 participants receiving FTC/TDF, plasma TDF concentrations and dried blood spot (DBS) intra-erythrocytic tenofovir-diphosphate (TFV-DP) were measured;
  - 64% of plasma samples contained detectable concentrations of TDF;
  - 48% contained concentrations of TDF expected for daily use.
- This suggests that the HPTN 084 study population was more adherent to daily oral Truvada than had been originally anticipated, likely conferring an even higher level of protection against HIV infection for Truvada-recipients than had been planned for in the original study design.

Safety Key Points

- Both CAB LA and FTC/TDF were safe and well tolerated in HPTN 084.
- Most adverse events were mild or moderate and balanced between arms.
- Injection Site Reactions (ISR) were reported by 130 (9.0%) participants in the FTC/TDF arm and 472 (32.0%) participants in the CAB arm:
  - Most ISRs were commonly mild or moderate pain and/or tenderness.
  - Zero participants in either arm discontinued injections due to injection-related adverse events.

Next Steps

What happens to participants now?

- Study participants will be informed of the study results and of which medication they were taking.
- Participants will be offered the opportunity to remain in the study, initially remaining on the active study medication that they were assigned to at the beginning of the study.
- Participants taking active FTC/TDF who wish to use CAB LA will be able to do so as soon as it is available.
- Participants who wish to may continue taking daily oral FTC/TDF.

Way Forward

- HPTN 083-01 and HPTN 084-01 are testing the safety, acceptability, and tolerability of CAB LA among adolescents (16, 17yrs)

- MUJHU site was activated for HPTN084-01

Availability of CAB LA for PrEP

- It is too early to know when CAB LA may be available for individuals outside of the HPTN084 study.

- The regulatory approval process for CAB LA requires several steps that need to occur first, including review and approval by the U.S. Food and Drug Administration and other regulatory agencies.

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And many other generous individuals and partners around the world

As of December 2019

Questions?

OK to share slides with attendees and public after Summit?

- **Please indicate Yes or No**
- **Yes**
- **No**